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## **Pathogenesis and Diagnosis of Food Hypersensitivity in Adults**

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### **Abstract**

Objective tools to diagnose local gastrointestinal (GI) inflammatory reactions in patients with food hypersensitivity are lacking. To fully appreciate the mechanisms mediating allergy-like reactions in the GI tract and for improvement of diagnostic techniques more knowledge is required.

The aims of this investigation were to (I) compare retrospectively a new approach for a more objective estimation of symptoms in double-blind placebo-controlled food challenge (DBPCFC) with the previous routine method of obtaining a diagnosis in adults; (II) to analyse the GI inflammation in adults with negative and positive skin prick test (SPT) and serum-IgE antibody with food hypersensitivity during symptomatic and asymptomatic periods and (III) in birch pollen allergic patients during and out of the birch pollen season; (IV) to assess markers of inflammation in duodenal biopsies, serum and faeces from these patients.

I: Three independent observers re-evaluated DBPCFC protocols with a new strategy for interpreting symptoms; inter-observer agreement was 100% and 97%. All patients previously diagnosed as positive were re-evaluated as positive. The new approach resulted in 34% and 38% being positive, compared with 22% by the previous method.

II and III: The investigation of inflammatory features in the duodenal mucosa of the food hypersensitive patients during exposure to offending food allergens showed significant increases of MBP+ eosinophils, IgE-bearing cells and T cells. Similar features were seen in birch pollen allergic patients during the birch pollen season, but not off-season. Healthy controls did not show such inflammatory signs. IL-4+ cells were increased in number, while IFN- $\gamma$  cells were reduced in the food hypersensitive patients when symptomatic compared to when asymptomatic, or to controls. The inflammatory pattern in the duodenal mucosa was similar in patients with negative and positive SPT/ serum-IgE antibodies whether challenged with foods or birch pollen allergens.

IV: During food challenge DBPCFC-positive adults with significant increase of abdominal pain, distension and flatulence, exhibited EPX levels in faeces. Such levels were more obvious for EPX compared with those of the markers of ECP and MPO. Individuals with a short duration of symptoms had significantly higher mean levels of EPX and MPO in faeces than those with a longer duration of symptoms.

Conclusions:

Subjective symptoms could be managed by using the pre-defined strategy allowing improved interpretations, i.e. independent of the observer. Patients with proven food

hypersensitivity and birch pollen allergic individuals during season showed increased numbers of inflammatory markers in the duodenal mucosa. The lack of serum-IgE and SPT positivity suggested a local reaction in the food hypersensitive patients. Local reactions to food components should be considered to enable a correct diagnosis. Our results give evidence for the presence and interplay between immunologically active cells in the airways and the GI tract in birch pollen allergic patients. Increased levels of eosinophil markers, in particular EPX, were observed in faeces from patients with food related GI-symptoms.

Key words: Birch pollen allergy, DBPCFC, Diagnosis, Duodenal mucosa, Eosinophils, Faecal samples, Food induced gastrointestinal hypersensitivity, IgE, Neutrophil MPO, T lymphocytes

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